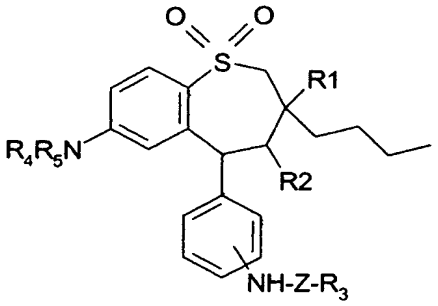
CLAIMS

1. A pharmaceutical composition for the prevention or treatment of Alzheimer's disease, comprising an effective amount of one or more compounds which are biliary acid reuptake inhibitors (BARI), and one or more pharmaceutically acceptable carriers, diluents or excipients, or a mixture thereof.

2. The composition as set forth in claim 1 wherein the BARI is a compound of formula (IA):



(IA)

wherein:

R^1 is methyl, ethyl, propyl or butyl;

R^2 is H, OH, NH_2, or NH-(C_1-C_6)alkyl;

R^3 is a saccharide, disaccharide, trisaccharide or quadrisaccharide radical, wherein said radicals are optionally mono- or polysubstituted with a sugar protective group;

R^4 is methyl, ethyl, propyl or butyl;

R^5 is methyl, ethyl, propyl or butyl;

Z is $-(C=O)_n-(C_0-C_{16})$-alkyl;

$-(C=O)_n-(C_0-C_{16})$-alkyl-NH; $-(C=O)_n-(C_0-C_{16})$-alkyl-O;

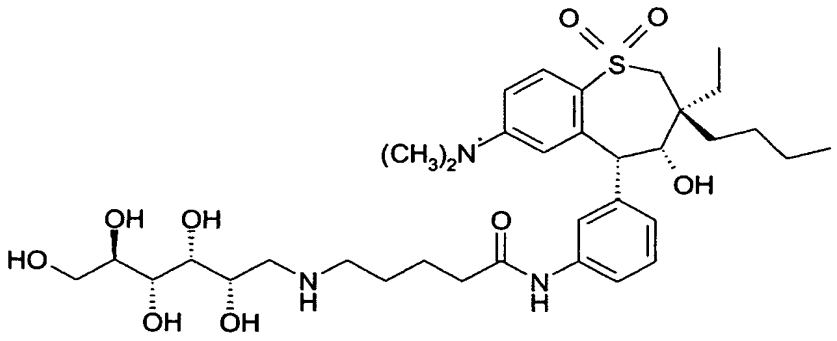
$-(C=O)_n-(C_0-C_{16})$-alkyl-$(C=O)_m-$; or a covalent bond;

n is 0 or 1;

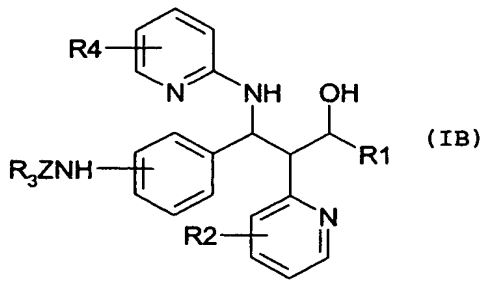
m is 0 or 1;

or a pharmaceutically acceptable addition salt thereof, or a physiologically functional derivative thereof.

3. The composition as set forth in claim 2 wherein the compound is having the following formula:



4. The composition as set forth in claim 1 wherein the BARI is a compound of formula (IB):



(IB)

wherein:

R^1 is phenyl or heteroaryl, wherein the aromatic or heteroaromatic ring is unsubstituted or is substituted with one to three independent radicals chosen from F, Cl, Br, I, -OH, $-CF_3$, $-NO_2$, $-NHR^9$, $-NR^9R^{10}$, -CHO, $-CO_2H$, $-CO_2R^{11}$, $-COR^{12}$, $-(C_1-C_6)$-alkyl-OH, $-(C_1-C_6)$-alkyl-OH-phenyl, $-(C_1-C_6)$-alkyl-CF_3, $-(C_1-C_6)$-alkyl-NO_2, $-(C_1-C_6)$-alkyl-CN, $-(C_1-C_6)$-alkyl-NH_2, $-(C_1-C_6)$-alkyl-NHR^9, $-(C_1-C_6)$-alkyl-NR^9R^{10}, $-(C_1-C_6)$-alkyl-CHO, $-(C_1-C_6)$-alkyl-CO_2H, $-(C_1-C_6)$-alkyl-CO_2R^{11}, $-(C_1-C_6)$-alkyl-COR^{12}, $-O-(C_1-C_6)$-alkyl-OH, $-O-(C_1-C_6)$-alkyl(-OH)-phenyl, $-O-(C_1-C_6)$-alkyl-CF_3, $-O-(C_1-C_6)$-alkyl-NO_2, $-O-(C_1-C_6)$-alkyl-CN, $-O-(C_1-C_6)$-alkyl-NH_2, $-O-(C_1-C_6)$-alkyl-NHR^9, $-O-(C_1-C_6)$-alkyl-NR^9R^{10}, $-O-(C_1-C_6)$-alkyl-CHO, $-O-(C_1-C_6)$-N-S_3H, $-S_2-CH_3$, $-O-(C_1-C_6)$-alkyl-$O-(C_1-C_6)$-alkylphenyl, $-(C_1-C_6)$-alkylthio or pyridyl, wherein one or more hydrogen(s) in the alkyl radicals may be optionally replaced by fluorine, and wherein phenyl or pyridyl may be unsubstituted or monosubstituted by methyl, methoxy or halogen;

R^2 is H, OH, $-CH_2OH$, -OMe, -CHO or $-NH_2$;

R^3 is a saccharide, disaccharide, trisaccharide or quadrisaccharide radical, wherein said radical may be unsubstituted or mono- or polysubstituted with a sugar protecting group, $HO-SO_2-$ or $(HO)_2-PO-$;

R^4 is H, methyl, F or -OMe;

R^9, R^{10}, R^{11}, and R^{12} are the same or different, and independently of each other are H or $-(C_1-C_8)$-alkyl;

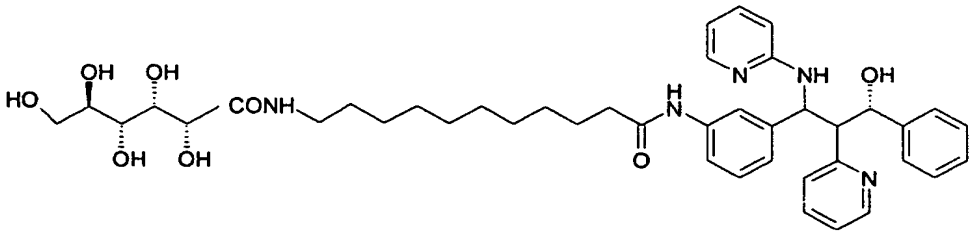
Z is a covalent bond or a group chosen from $-NH-(C_0-C_{16})$-alkyl-CO-, $-O-(C_0-C_{16})$-alkyl-CO-, $-(CO)_m-(C_0-C_{16})$-alkyl-$(CO)_n$-, an amino acid residue, a diamino acid residue, wherein the amino acid residue or diamino acid residue is unsubstituted, or mono- or polysubstituted by an amino acid-protecting group;

n is 0 or 1;

m is 0 or 1;

or a pharmaceutically acceptable addition salt, or a physiologically functional derivative thereof.

5. The composition as set forth in claim 4 wherein the compound is having the following formula:



6. The composition as set forth in claim 1 which is administered orally.

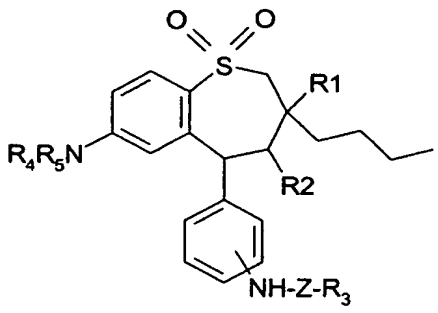
7. The composition as set forth in claim 6 which contains from about 0.02 to about 50 mg of the biliary acid reuptake inhibitor.

8. The composition as set forth in claim 1 wherein one or more biliary acid reuptake inhibitors are combined with one or more compounds chosen from HMG-CoA reductase inhibitors, cholesterol uptake inhibitors, cholesterol synthesis inhibitors or γ and β APP secretase inhibitors.

9. The composition as set forth in claim 8 wherein the various active ingredients are administered simultaneously, separately or spaced out over time.

10. A pharmaceutical composition for the prevention or treatment of Alzheimer's disease, comprising an effective amount of one or more compounds which reduce the plasma cholesterol levels without the need to be absorbed in the body after their oral administration, and one or more pharmaceutically acceptable carriers, diluents or excipients, or a mixture thereof.

11. The composition as set forth in claim 10 wherein the compound is of the following formula (IA):



(IA)

wherein:

R^1 is methyl, ethyl, propyl or butyl;

R^2 is H, OH, NH_2, or NH-$(C_1$-$C_6)$alkyl;

R^3 is a saccharide, disaccharide, trisaccharide or quadrisaccharide radical, wherein said radicals are optionally mono- or polysubstituted with a sugar protective group;

R^4 is methyl, ethyl, propyl or butyl;

R^5 is methyl, ethyl, propyl or butyl;

Z is $-(C=O)_n-(C_0-C_{16})$-alkyl;

$-(C=O)_n-(C_0-C_{16})$-alkyl-NH; $-(C=O)_n-(C_0-C_{16})$-alkyl-O;

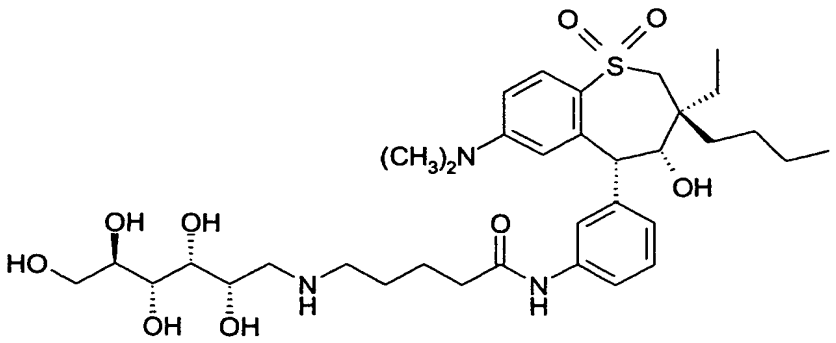
$-(C=O)_n-(C_0-C_{16})$-alkyl-$(C=O)_m-$; or a covalent bond;

n is 0 or 1;

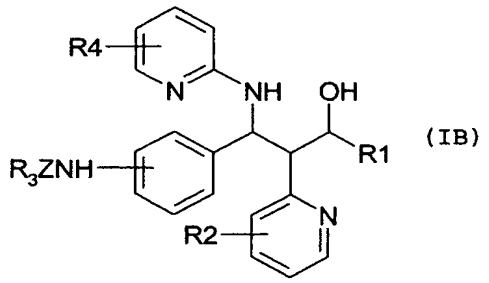
m is 0 or 1;

or a pharmaceutically acceptable addition salt thereof, or a physiologically functional derivative thereof.

12. The composition as set forth in claim 11 wherein the compound is having the following formula:



13. The composition as set forth in claim 10 wherein the compound is of the following formula (IB):



(IB)

wherein:

R^1 is phenyl or heteroaryl, wherein the aromatic or heteroaromatic ring is unsubstituted or is substituted with one to three independent radicals chosen from F, Cl, Br, I, -OH, $-CF_3$, $-NO_2$, $-NHR^9$, $-NR^9R^{10}$, -CHO, $-CO_2H$, $-CO_2R^{11}$, $-COR^{12}$, $-(C_1-C_6)$-alkyl-OH, $-(C_1-C_6)$-alkyl-OH-phenyl, $-(C_1-C_6)$-alkyl-CF_3, $-(C_1-C_6)$-alkyl-NO_2, $-(C_1-C_6)$-alkyl-CN, $-(C_1-C_6)$-alkyl-NH_2, $-(C_1-C_6)$-alkyl-NHR^9, $-(C_1-C_6)$-alkyl-NR^9R^{10}, $-(C_1-C_6)$-alkyl-CHO, $-(C_1-C_6)$-alkyl-CO_2H, $-(C_1-C_6)$-alkyl-CO_2R^{11}, $-(C_1-C_6)$-alkyl-COR^{12}, $-O-(C_1-C_6)$-alkyl-OH, $-O-(C_1-C_6)$-alkyl(-OH)-phenyl,

$-O-(C_1-C_6)-alkyl-CF_3$, $-O-(C_1-C_6)-alkyl-NO_2$, $-O-(C_1-C_6)-alkyl-CN$, $-O-(C_1-C_6)-alkyl-NH_2$, $-O-(C_1-C_6)-alkyl-NHR^9$, $-O-(C_1-C_6)-alkyl-NR^9R^{10}$, $-O-(C_1-C_6)-alkyl-CHO$, $-O-(C_1-C_6)-N-S_3H$, $-S_2-CH_3$, $-O-(C_1-C_6)-alkyl-O-(C_1-C_6)-alkylphenyl$, $-(C_1-C_6)-alkylthio$ or pyridyl, wherein one or more hydrogen(s) in the alkyl radicals may be optionally replaced by fluorine, and wherein phenyl or pyridyl may be unsubstituted or monosubstituted by methyl, methoxy or halogen;

R^2 is H, OH, $-CH_2OH$, -OMe, -CHO or $-NH_2$;

R^3 is a saccharide, disaccharide, trisaccharide or quadrisaccharide radical, wherein said radical may be unsubstituted or mono- or polysubstituted with a sugar protecting group, $HO-SO_2-$ or $(HO)_2-PO-$;

R^4 is H, methyl, F or -OMe;

R^9, R^{10}, R^{11}, and R^{12} are the same or different, and independently of each other are H or $-(C_1-C_8)-alkyl$;

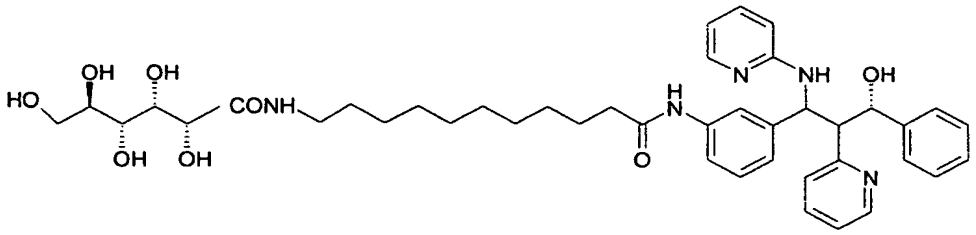
Z is a covalent bond or a group chosen from $-NH-(C_0-C_{16})-alkyl-CO-$, $-O-(C_0-C_{16})-alkyl-CO-$, $-(CO)_m-(C_0-C_{16})-alkyl-(CO)_n-$, an amino acid residue, a diamino acid residue, wherein the amino acid residue or diamino acid residue is unsubstituted, or mono- or polysubstituted by an amino acid-protecting group;

n is 0 or 1;

m is 0 or 1;

or a pharmaceutically acceptable addition salt, or a physiologically functional derivative thereof.

14. The composition as set forth in claim 13 wherein the compound is having the following formula:



15. The composition as set forth in claim 10 which is administered orally.

16. The composition as set forth in claim 15 which contains from about 0.02 to about 50 mg of the compound.

17. The composition as set forth in claim 10 wherein one or more biliary acid reuptake inhibitors are combined with one or more compounds chosen from HMG-CoA reductase inhibitors, cholesterol uptake inhibitors, cholesterol synthesis inhibitors or γ and β APP secretase inhibitors.

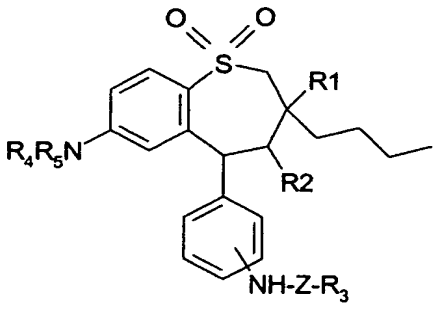
18. The composition as set forth in claim 17 wherein

the various active ingredients are administered simultaneously, separately or spaced out over time.

19. A method for the prevention or treatment of Alzheimer's disease in a patient at risk of developing said disease or in the course of developing said disease, comprising administering to said patient an effective amount of a compound having a hypocholesterolemic activity wherein said compound does not penetrate into the body after its oral administration.

20. The method as set forth in claim 19 wherein the compound having a hypocholesterolemic activity and not penetrating into the body is a biliary acid reuptake inhibitor.

21. The method as set forth in claim 20, wherein the biliary acid reuptake inhibitor is a compound of formula (IA):



(IA)

wherein:

R^1 is methyl, ethyl, propyl or butyl;

R^2 is H, OH, NH_2, or NH-$(C_1$-$C_6)$alkyl;

R^3 is a saccharide, disaccharide, trisaccharide or quadrisaccharide radical, wherein said radicals are optionally mono- or polysubstituted with a sugar protective group;

R^4 is methyl, ethyl, propyl or butyl;

R^5 is methyl, ethyl, propyl or butyl;

Z is $-(C=O)_n-(C_0-C_{16})$-alkyl;

$-(C=O)_n-(C_0-C_{16})$-alkyl-NH; $-(C=O)_n-(C_0-C_{16})$-alkyl-O;

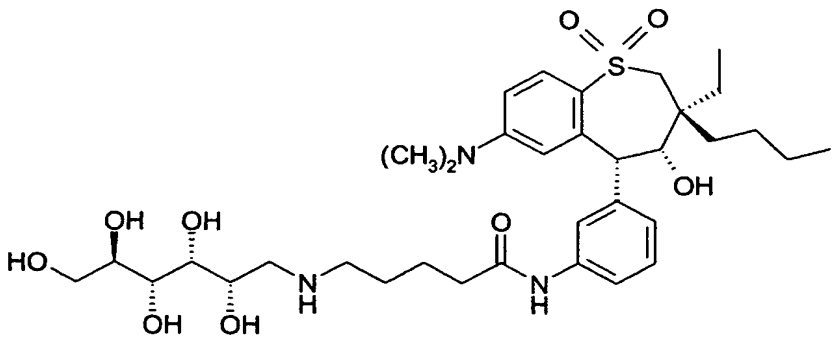
$-(C=O)_n-(C_0-C_{16})$-alkyl-$(C=O)_m-$; or a covalent bond;

n is 0 or 1;

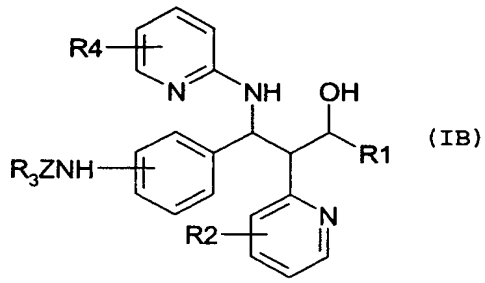
m is 0 or 1;

or a pharmaceutically acceptable addition salt thereof, or a physiologically functional derivative thereof.

22. The method as set forth in claim 21 wherein the compound is having the following formula:



23. The method as set forth in claim 20 wherein the biliary acid reuptake inhibitor is a compound of formula (IB):



wherein:

R^1 is phenyl or heteroaryl, wherein the aromatic or heteroaromatic ring is unsubstituted or is substituted with one to three independent radicals chosen from F, Cl, Br, I, -OH, $-CF_3$, $-NO_2$, $-NHR^9$, $-NR^9R^{10}$, -CHO, $-CO_2H$, $-CO_2R^{11}$, $-COR^{12}$, $-(C_1-C_6)$-alkyl-OH, $-(C_1-C_6)$-alkyl-OH-phenyl, $-(C_1-C_6)$-alkyl-CF_3, $-(C_1-C_6)$-alkyl-NO_2, $-(C_1-C_6)$-alkyl-CN, $-(C_1-C_6)$-alkyl-NH_2, $-(C_1-C_6)$-alkyl-NHR^9, $-(C_1-C_6)$-alkyl-NR^9R^{10}, $-(C_1-C_6)$-alkyl-CHO, $-(C_1-C_6)$-alkyl-CO_2H, $-(C_1-C_6)$-alkyl-CO_2R^{11}, $-(C_1-C_6)$-alkyl-COR^{12}, $-O-(C_1-C_6)$-alkyl-OH, $-O-(C_1-C_6)$-alkyl(-OH)-phenyl, $-O-(C_1-C_6)$-alkyl-CF_3, $-O-(C_1-C_6)$-alkyl-NO_2, $-O-(C_1-C_6)$-alkyl-CN, $-O-(C_1-C_6)$-alkyl-NH_2, $-O-(C_1-C_6)$-alkyl-NHR^9, $-O-(C_1-C_6)$-alkyl-NR^9R^{10}, $-O-(C_1-C_6)$-alkyl-CHO, $-O-(C_1-C_6)$-N-S_3H, $-S_2-CH_3$, $-O-(C_1-C_6)$-alkyl-$O-(C_1-C_6)$-alkylphenyl, $-(C_1-C_6)$-alkylthio or pyridyl, wherein one or more

hydrogen(s) in the alkyl radicals may be optionally replaced by fluorine, and wherein phenyl or pyridyl may be unsubstituted or monosubstituted by methyl, methoxy or halogen;

R^2 is H, OH, $-CH_2OH$, -OMe, -CHO or $-NH_2$;

R^3 is a saccharide, disaccharide, trisaccharide or quadrisaccharide radical, wherein said radical may be unsubstituted or mono- or polysubstituted with a sugar protecting group, $HO-SO_2-$ or $(HO)_2-PO-$;

R^4 is H, methyl, F or -OMe;

R^9, R^{10}, R^{11}, and R^{12} are the same or different, and independently of each other are H or $-(C_1-C_8)-alkyl$;

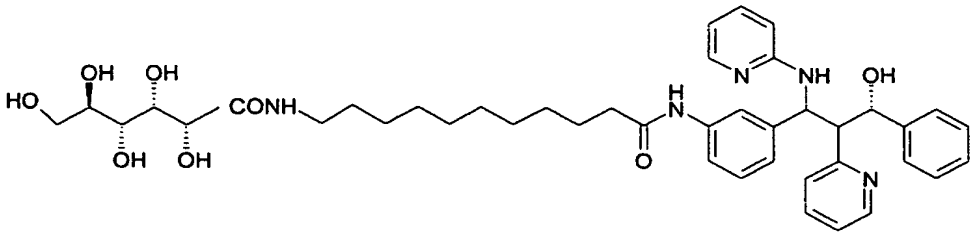
Z is a covalent bond or a group chosen from $-NH-(C_0-C_{16})-alkyl-CO-$, $-O-(C_0-C_{16})-alkyl-CO-$, $-(CO)_m-(C_0-C_{16})-alkyl-(CO)_n-$, an amino acid residue, a diamino acid residue, wherein the amino acid residue or diamino acid residue is unsubstituted, or mono- or polysubstituted by an amino acid-protecting group;

n is 0 or 1;

m is 0 or 1;

or a pharmaceutically acceptable addition salt, or a physiologically functional derivative thereof.

24. The method as set forth in claim 23 wherein the compound is having the following formula:



25. The method as set forth in claim 19 wherein the compound is administered orally.

26. The method as set forth in claim 25 wherein the compound is administered in an amount from about 0.02mg to about 50 mg.

27. The method as set forth in claim 20 wherein one or more biliary acid reuptake inhibitors are administered in combination with one or more compounds chosen from HMG-CoA reductase inhibitors, cholesterol uptake inhibitors, cholesterol synthesis inhibitors or γ and β APP secretase inhibitors.

28. The composition as set forth in claim 27 wherein the various active ingredients are administered simultaneously, separately or spaced out over time.